UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/743,746	01/16/2001	Gunter Schmidt	PM 0276611	7741

909 7590 06/08/2005

PILLSBURY WINTHROP SHAW PITTMAN, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 06/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/743,746	SCHMIDT ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8,10-31 and 35-39* is/are pending in the application.

4a) Of the above claim(s) *3,13-19,23-30 and 35-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6,8,10-12,20-22 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

3100.

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/21/05 has been entered. Claims 1-6, 8, 10-31 and 35-39 were pending. Applicants amended claim 1. No claims were added or canceled. Therefore, claims 1-6, 8, 10-31 and 35-39 are still pending. Claims 3, 13-19, 23-30 and 35-39 are drawn to non-elected species and/or inventions and thus these claims remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), there being no allowable generic claim. Therefore, claims 1, 2, 4-6, 8, 10-12, 20-22 and 31 are examined on the merits.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

Withdrawn Objections/Rejections

2. The Written Description and Enablement rejections under 35 U.S.C. § 112, first paragraph are withdrawn in view of Applicants' arguments and/or amendments. All rejections are withdrawn in view of Applicants' arguments and/or amendments.

Maintained Rejections

Claims Rejections - 35 U.S.C. 102 - maintained

3. Claims 1, 2, 4-6, 8, 10-12, 20 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Nothnagel (Nothnagel, E. A. "Synthesis and characterization of fluorescent Lucifer yellow-lipid conjugates" Biochimica et Biophysica Acta **1989**, 980(2), 209-219).

For ***claim 1***, Nothnagel (see entire document) disclose methods for synthesizing and using fluorescent Lucifer yellow-lipid conjugates (see Nothnagel, abstract), which anticipates claim 1. For example, Nothnagel disclose providing a compound in which the analyte is attached by a cleavable linker to a reporter group relatable to the analyte having the formula shown in claim 1 (e.g., see Nothnagel, figure 1, schematic B showing a compound with formula LY-SO_2-CH_2-CH_2-$DC_{12:0}$PE). In this scenario, the Lucifer Yellow Dye ("LY") represents the "reporter" and the $DC_{12:0}$PE represents the "analyte." further disclose cleaving the reporter group from the analyte (e.g., see Nothnagel, figure 2 wherein the $DC_{12:0}$PE "analyte" is cleaved from the LY "reporter" via FAB-MS i.e., the peak at 578 corresponds to the "cleaved" $DC_{12:0}$PE analyte peak). Finally, Nothnagel disclose identifying the reporter group, thereby characterizing the analyte (e.g., see Nothnagel, figure 2 wherein the parent ion and fragment ions that contain the FY reporter are "identified" and used to "identify" the lipid analyte via comparison of molecular weights and known 1:1 correlation between reporter and analyte). Please note that there are many other variations for the analyte and/or reporter that also read on Applicants' claims. For example, the "analyte" could be a "12:0 fatty acid side chain" instead of the $DC_{12:0}$PE mentioned above or the phoshphatidic acid portion ("PA") of the molecule

(e.g., see Nothnagel, figure 2 wherein the peaks at 946 and 346 represent "lyso" derivatives of $DC_{12:0}PE$ wherein fatty acid side chain "analytes" are cleaved from the reporter).

For ***claim 2***, Nothnagel disclose a covalent linkage between the analyte and/or reporter group and the cleavable linker (e.g., see figure 2 showing the cleavage of a covalent bond when the DC12:0PE signal is generated at mass 578).

For ***claim 4-6***, Nothnagel disclose a substituted phenyl wherein R^2, R^4, R^5 and R^6 are hydrogen and R^3 is LY (e.g., see Nothnagel, figure 1, scheme B wherein a phenyl ring connects the LY to the SO_2-CH_2-CH_2-$DC_{12:0}PE$ i.e., LY-phenyl-SO_2-CH_2-CH_2-$DC_{12:0}PE$).

For ***claim 8***, Nothnagel disclose -NR^1- wherein R^1 is a hydrogen (e.g., see Nothnagel, figure 1, scheme B showing -SO_2-CH_2-CH_2-N(H)-CH_2-CH_2-).

For ***claims 11-12***, Nothnagel disclose LY-phenyl-SO_2-CH_2-CH_2-N(H)-CH_2-CH_2-$DC_{12:0}PA$ wherein "PA" represents the phosphatidic acid portion of the molecule (e.g., see Nothnagel, figure 1, scheme B). In this scenario, X' is PA, the "handle" connecting PA to N-R^1 is -CH_2-CH_2-, R^1 is hydrogen, the "handle" connecting SO_2 to X is a covalent bond and X is LY. Please note that claim 12 has been interpreted as depending on claim 11.

For ***claims 20 and 31***, Nothnagel disclose detecting the reporter using FAB-MS and its cleavage products (e.g., see Nothnagel, figure 2).

Response

4. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "claim 1 has been amended to refer to a method to 'identify an analyte' rather than to 'characterize an analyte'" (e.g., see 3/21/05 Response, page 13, section IV), which presumably distinguishes the amended claims over Nothnagel.

[2] Applicants argue, "Claim 1 has also been amended to define that the cleavage take place by beta elimination between the R' group and the adjacent carbon atom (e.g., see 3/21/05 Response, page 13, section IV), which presumably distinguishes the claimed the amended claims over Nothnagel.

This is not found persuasive for the following reasons:

[1] The Examiner respectfully disagrees. There is a 1:1 correlation between the fluorescent dye and lipid molecule (i.e., they are linked together in a 1:1 ration by a cleavable linker). Thus, the identification of one (e.g., the reporter) necessarily leads to the identification of the other (e.g., the analyte). Here, the reporter group has been identified in the mass spectrometer (e.g., see peak at 450 in figure 2) and, as a result, the lipid analyte is unequivocally identified.

[2] The Examiner contends that the cleavage (e.g., peaks at 450, 946, 578, 396 in figure 2) resulted from beta cleavage because Nothnagel is the same cleavable linkers as currently

claimed (e.g., the -Ph-SO_2-CH_2-CH_2-NH-) with the same "electron withdrawing" group at the R^1 position (e.g., see claims 11-12) in a mass spectrometer (e.g., see claim 20). Thus, said cleavage must occur by the same mechanism. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01. The Office does not have the facilities to make such a comparison and the burden is on the applicants to establish the difference. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Accordingly, the 35 U.S.C. §102 rejection cited above is hereby maintained.

New Rejections

Claim Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 2, 4-6, 8, 10-12, 20-22 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. ***Claims 8 and 11*** recite "electron withdrawing" group and/or substituent. The term "electron withdrawing" is a relative term, which renders the claim indefinite and/or unclear. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. See also MPEP § 2173.05(b). For example, Applicants state that hydrogen falls within the scope of an electron withdrawing substituent for the R^1 position (e.g., see claim 12 disclosing hydrogen, which further limits the electron withdrawing group R^1 disclosed in claim 11). However, hydrogen would appear to be functioning as an "electron donating" group in this case because it has a smaller electronegativity value than the nitrogen atom to which it is attached (e.g., see Electronegativity chart 5/25/05 http://web.mit.edu/3.091/www/pt/per8.html wherein H = 2.1 and N = 3.04). If Applicants contend that an "electron withdrawing" group can have any electronegativity value, then it is not clear how an "electron withdrawing" group differs from the "donating" group especially in light of the discussion mentioned above wherein the hydrogen appears to be acting as an "electron donating" group. It is also noted that while applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). Consequently, the metes and bounds of the claimed invention cannot be determined. Thus, claims 8, 11 and all dependent claims are rejection under 35 U.S.C. 112, second paragraph.

B. For ***claim 1***, the phrase "wherein the cleavage takes place by beta-elimination between the R' group and the adjacent carbon atom" is vague and indefinite when used in conjunction with the claimed R-SO_n-CH_2-CH_2-R' molecules because it is not clear which of said molecules will undergo such a reaction. For example, Applicants state that the fluorescent-lipid conjugate in Nothnagel does not undergo beta-elimination (e.g., see 3/21/05 Response, page 13, section IV). However, this fluorescent-lipid conjugate falls within the scope of Applicants' claims and, as a result, should undergo such a reaction. A chemical compound and its properties are inseparable. The court has held that if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). However, Applicants' state that a compound and its properties are separable in this case (when referring to the Nothnagel reference), which directly refutes the holding in *In re Spada*. Consequently, a person of skill in the art cannot immediately envision all the possible chemical structures for a compound with this function (i.e., beta elimination). See *ex parte Pulvari* (POBA 1966) 157 USPQ 169. Therefore, the metes and bound of the claimed invention cannot be determined and, as a result, claim 1 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1, 2, 4-6, 8, 10-12, 20-22 and 31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-39 (especially claims 19, 20, 28, 31 and 39) of U.S. Patent No. 6,582,916 B1 (referred to herein as '916). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986). Although the conflicting claims are not identical, they are not patentably distinct from each other because, for example, claims 1, 2, 4-6, 8, 10-12, 20-22 and 31 are generic to all that is recited in claims 1-39 of '916. That is, claims 1-39 of '916 fall entirely within the scope of claim 1, 2, 4-6, 8, 10-12, 20-22 and 31 of the present application or, in other words, claims 1, 2, 4-6, 8, 10-12, 20-22 and 31 of the present application are anticipated by claims 1-39 of '916.

Specifically, **[1]** both references disclose providing a compound in which the analyte is attached by a cleavable linker to a reporter group relatable to the analyte (e.g., compare claim 1 of the present application disclosing R-SO_n-CH_2-CH_2-R' to claims 27, 28, 31 and 39 of '916

disclosing N-L-M and -Ph-SO_2-CH_2-CH_2-N(-R)- wherein the -SO_2-CH_2-CH_2- of '916 is identical to the compound disclose in claim 1 of the present application when n=2; N falls within the scope of R/R' because a nucleic acid is an analyte; M falls within the scope of R/R' because M is a mass marker), **[2]** both references disclose a biological analyte comprising a nucleophile selected from the group consisting of amines, thiols and hydroxyls (e.g., compare claim 1 of the present application to claim 27 of '916 disclosing a "nucleic acid" analyte that falls within the scope of claim 1 because it is a biological analyte that possesses hydroxyl groups), **[3]** both references disclose cleaving the reporter group from the analyte (e.g., compare claim 1 of the present application to claim 27 of '916 wherein both disclose a cleavable linker; see also claim 32, "further comprising heating the compound to cleave the mass marker from the molecule"), **[4]** '916 does not specifically recite that the cleavage takes place via a beta-elimination as stated in claim 1 of the present application, but the Examiner contends that this would be an inherent feature of the because both references disclose the same preferred cleavable linkers (e.g., compare claim 11 of the present application to claim 28 of '916 wherein -Ph-SO_2-CH_2-CH_2-N(-R)- is disclosed in each case) and both references disclose cleaving said preferred cleavable linker using a mass spectrometer (e.g., compare claim 31 of the present application to claim 33 of '916) and **[5]** both applications disclose identifying the reporter group by mass spectrometry and determining the mass-to-charge ration of the reporter, thereby identifying the analyte (e.g., compare claim 1 of the present application to claims 23 of '916). The '916 patent also discloses many other embodiments that either overlap in scope and/or anticipate the claimed invention including **[6]** the use of a "polyether" mass marker including poly "aryl" ethers with fluorine substituents (e.g., compare claim 21-23 of the present application to claims 8, 10 and 11 of '916).

8. Claims 1, 2, 4-6, 8, 10-12, 20-22 and 31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-45 (especially claims 19, 20, 28, 31 and 39) of U.S. Patent No. 6,287,780 B1 (referred to herein as '780). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986). Although the conflicting claims are not identical, they are not patentably distinct from each other because, for example, claims 1, 2, 4-6, 8, 10-12, 20-22 and 31 are generic to all that is recited in claims 1-45 of '780. That is, claims 1-45 of '780 fall entirely within the scope of claim 1, 2, 4-6, 8, 10-12, 20-22 and 31 of the present application or, in other words, claims 1, 2, 4-6, 8, 10-12, 20-22 and 31 of the present application are anticipated by claims 1-45 of '780.

Specifically, **[1]** both references disclose providing a compound in which the analyte is attached by a cleavable linker to a reporter group relatable to the analyte (e.g., compare claim 1 of the present application disclosing R-SO_n-CH_2-CH_2-R' to claims 13, 15 and 22 of '780 disclosing N-L-M and -Ph-SO_2-CH_2-CH_2-N(-R)- wherein the -SO_2-CH_2-CH_2- of '780 is identical to the compound disclose in claim 1; N falls within the scope of R/R' because a nucleic acid is an analyte; M falls within the scope of R/R' because M is a mass marker), **[2]** both references disclose a biological analyte comprising a nucleophile selected from the group consisting of

amines, thiols and hydroxyls (e.g., compare claim 1 of the present application to claim 13 of '780 disclosing a "nucleic acid" analyte that falls within the scope of claim 1 because it is a biological analyte that possesses hydroxyl groups), **[3]** both references disclose cleaving the reporter group from the analyte (e.g., compare claim 1 of the present application to claim 15 of '780 wherein both disclose a cleavable linker), **[4]** '780 does not specifically recite that the cleavage takes place via a beta-elimination as stated in claim 1 of the present application, but the Examiner contends that this would be an inherent feature of the because both references disclose the same preferred cleavable linkers (e.g., compare claim 11 of the present application to claim 22 of '780 wherein -Ph-SO_2-CH_2-CH_2-N(-R)- is disclosed in each case) and both references disclose cleaving said preferred cleavable linker using a mass spectrometer (e.g., compare claim 31 of the present application to claim 33 of '780) and **[5]** both applications disclose identifying the reporter group by mass spectrometry and determining the mass-to-charge ration of the reporter, thereby identifying the analyte (e.g., compare claim 1 of the present application to claims 33 of '780). The '780 patent also discloses many other embodiments that either overlap in scope and/or anticipate the claimed invention including **[6]** the use of a "polyether" mass marker including poly "aryl" ethers with fluorine substituents (e.g., compare claim 21-23 of the present application to claims 2-8 of '780).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
May 24, 2005

BENNETT CELSA
PRIMARY EXAMINER